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Influence of the morphology of lysozyme-shelled microparticles on the cellular association, uptake and degradation in SKBR3 cells

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The application of nanomedicine for cancer therapy has received considerable attention in recent years. The key issue is to achieve the desired concentration of therapeutic agents in tumor sites, thereby destroying cancerous cells while minimizing damage to normal cells. To pursue this approach, biomaterial science has stepped into the formulation of smart materials and miniaturized drug delivery devices [1].

The ultrasound assisted self-assembly and crosslinking of lysozyme at the water-air and water-perfluorohexane interface is shown to produce lysozyme-shelled hollow microbubbles (LSMBs) and microcapsules (LSMCs) [2, 3].

Herein, we report on the interaction of LSMBs and LSMCs with human breast adenocarcinoma cells (SKBR3). Biocompatibility of microcapsules and microbubbles has been evaluated by MTT test. The cellular internalization kinetics of LSMBs and LSMCs and the effects on cell cycle were evaluated using flow cytometry. LSMBs and LSMCs were phagocyted by cells within 2 hours without exerting a cytotoxic activity. Internalization of microparticles and degradation within the cell were also monitored by confocal analysis (Figure 1). Cell membrane integrity and cell cycle progression were not affected by LSMBs and LSMCs uptake. These studies have shown that the positively charged LSMBs and LSMCs were not cytotoxic and can be readily internalized and degraded by SKBR3 cells. LSMBs and LSMCs showed a different uptake kinetics and intracellular degradation pattern due to differences in the arrangement of protein at the air-liquid or oil-liquid interfaces. Furthermore, scanning electron microscopy (SEM) analysis was used to gain understanding on the mechanism of cell-microparticle interaction. A strong adhesion of microparticles on cell surface was observed confirming the absence of cytotoxic effects along with the maintenance of cell integrity, even when numerous particles were laying on the cell surface (Figure 2).

These results highlight the potential uses of LSMBs and LSMCs as ultrasound responsive platforms suited for biomedical and pharmaceutical applications.

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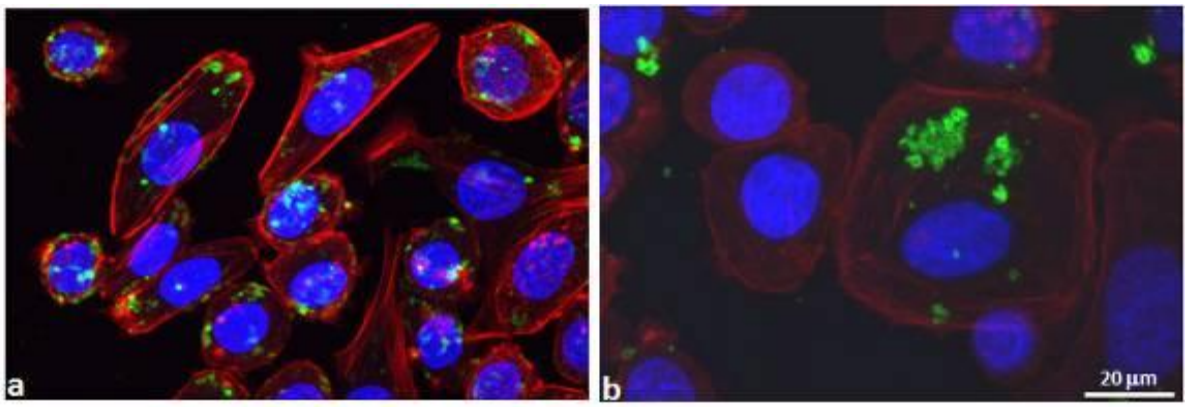

Figure 1. Confocal microscopy images of internalized microparticles. SKBR3 cells were incubated for 2 hours with LSMB-FITC (a) and LSMC-FITC (b). Green, red and blue indicate FITC-conjugated microparticles, actin filaments and nuclei stained with Hoechst 33342, respectively. LSMBs and LSMCs appear to be efficiently internalized by the cells.

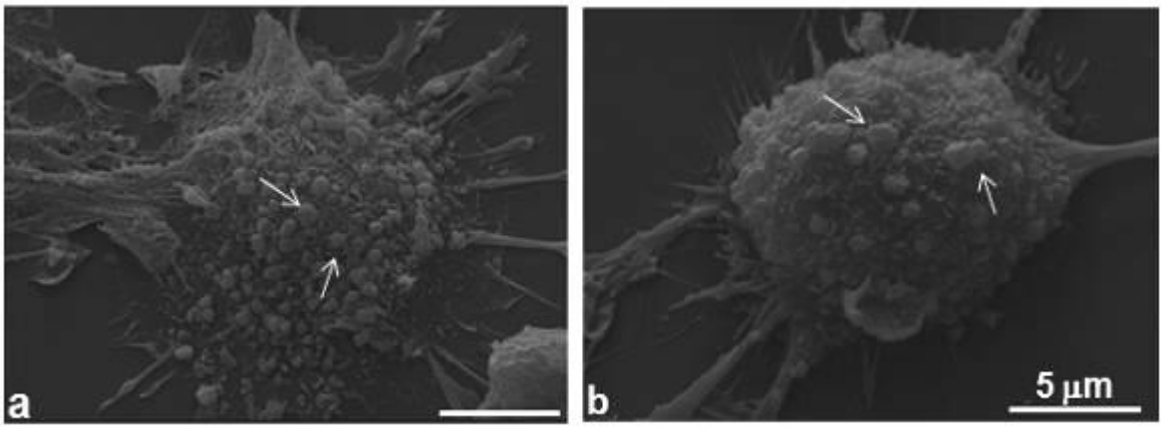

Figure 2. Scanning electron microscopy images of SKBR3 cells after incubation with LSMBs (a, arrows) and LSMCs (b, arrows) after 2 hours of incubation.